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CONTRACTING ORGANIZATION: Regents of University of California
Davis, CA 95616

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14. ABSTRACT The major objective of this research effort was to create new sensing technologies and perform preliminary studies prior to rapid transition to testing in blast TBI models. This project proposed to use miniaturized, state-of-the-art pressure/temperature sensors engineered at LLNL to measure the immediate increases in ICP combined with longer-term measurements of biological ICP and intracranial temperature. The experience gathered from this seed proposal provided valuable data on sensor placement, long-term brain tissue responses to implanted sensors, and sensor capability of dual measurement of biologic ICP and impact pressure transients that will be directly applicable to subsequent transition into blast TBI animal models.					
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Introduction:

The major objective of this research effort was to create new sensing technologies and perform preliminary studies prior to rapid transition to testing in blast TBI models. This project proposed to use miniaturized, state-of-the-art pressure/temperature sensors engineered at LLNL to measure the immediate increases in ICP combined with longer-term measurements of biological ICP and intracranial temperature. The experience gathered from this seed proposal provided valuable data on sensor placement, long-term brain tissue responses to implanted sensors, and sensor capability of dual measurement of biologic ICP and impact pressure transients that will be directly applicable to subsequent transition into blast TBI animal models.

Keywords:

Pressure Sensors, Traumatic Brain Injury, ICP, fluid percussion, blast TBI, Temperature

Accomplishments:**What were the major goals of the project?**

The first major goal of this project was to develop miniaturized, state-of-the-art pressure/temperature sensors engineered at LLNL to measure the immediate increases in ICP combined with longer-term measurements of biological ICP and intracranial temperature. The second major goal of this project was to apply this new sensing technology to measure pressure changes in the brain upon exposure to fluid percussion TBI in rats and blast TBI models.

What was accomplished under these goals?

We have made substantial progress on sensor development activities this quarter. Dr. Kotovsky has successfully produced test-ready sensors with a range of diaphragm diameters (200 - 1000 μm). Diaphragm diameter should affect sensitivity of the sensors. These wafer-scale, absolute pressure sensors have an ultra-thin form factor (thickness 90 μm prior to packaging and 130 μm after final packaging). The new sensors were designed to measure absolute pressure by modifying the original contact stress sensor design to create a reference cavity; a trapped volume of gas that is hermetically sealed within the device. The new sensors pre-define the pressure sensor's reference cavity within the Silicon-on-insulator (SOI) wafer. The pre-definition provides a variety of advantages to the overall process:

- The reference volume cavity definition requires a plasma etch that is a challenging operation to perform on a thinned substrate, performing this etch at the start of the SOI build pushes the process to a thick-wafer operation simplifying the processing significantly
- Pushing the reference volume cavity formation to the start of the process reduces yield risk by placing the most difficult process at the start of the fabrication (least substrate added-value)

- Producing the reference volume cavity requires a hermetic seal that requires a high temperature operation that is difficult to perform later in the process once metals are on the substrate
- Pre-definition of the reference volume cavity paves the way for no-backside processing of thinned substrates, increasing the overall yield of the process
- Etching of the reference volume cavities prior to metallization keeps the etching process CMOS clean
- Commercialization of the sensor is aided by this process as use of CMOS-clean commercial foundries will not be restricted

Bench calibration and testing of sensitivity have begun. Five new sensors with diaphragm diameters of 200, 400, 600, 800, and 1000 μm (Figures 1 & 2) are currently undergoing testing and calibration to determine the optimum diaphragm diameter for subsequent in-animal testing. The new sensors have been packaged with an encapsulating layer of Kapton to protect the sensor diaphragm and electrical connections from body fluids.

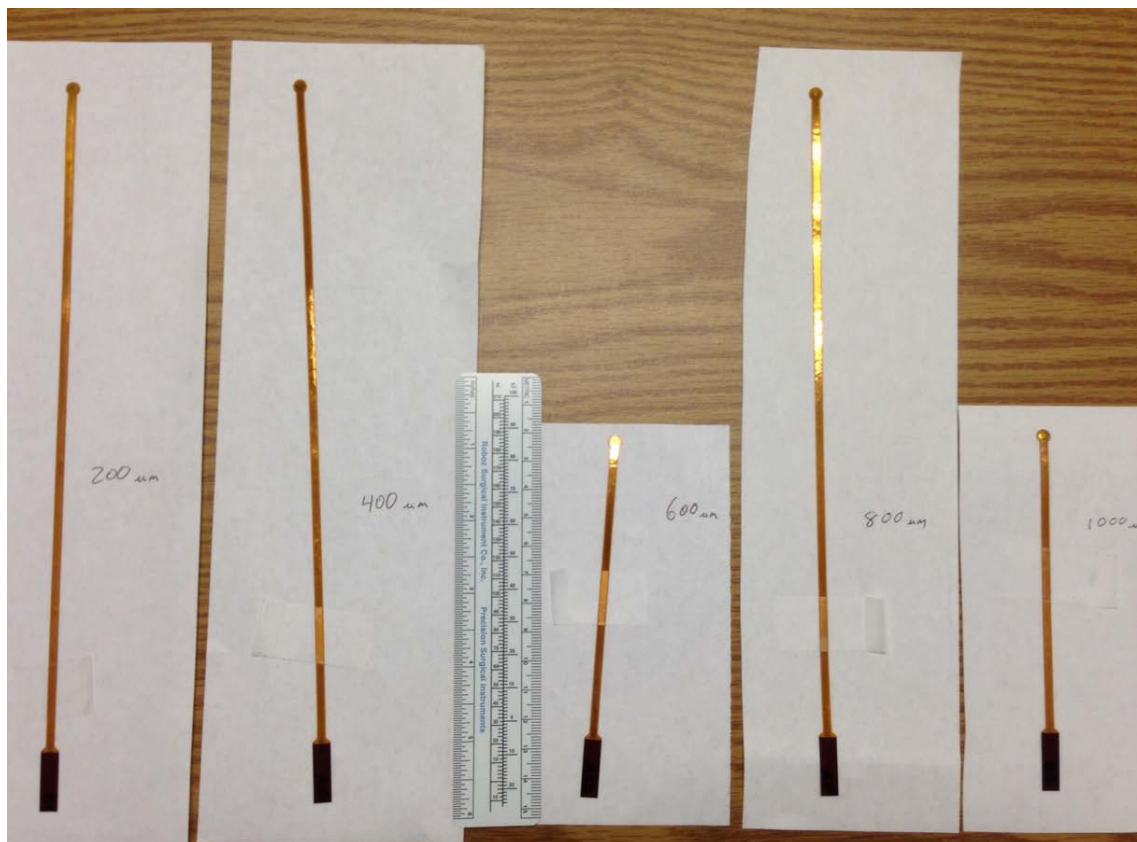


Figure 1. Sensors with different diaphragm diameters. The overall length of the sensor and connecting contact strip are either 13 or 25 mm.

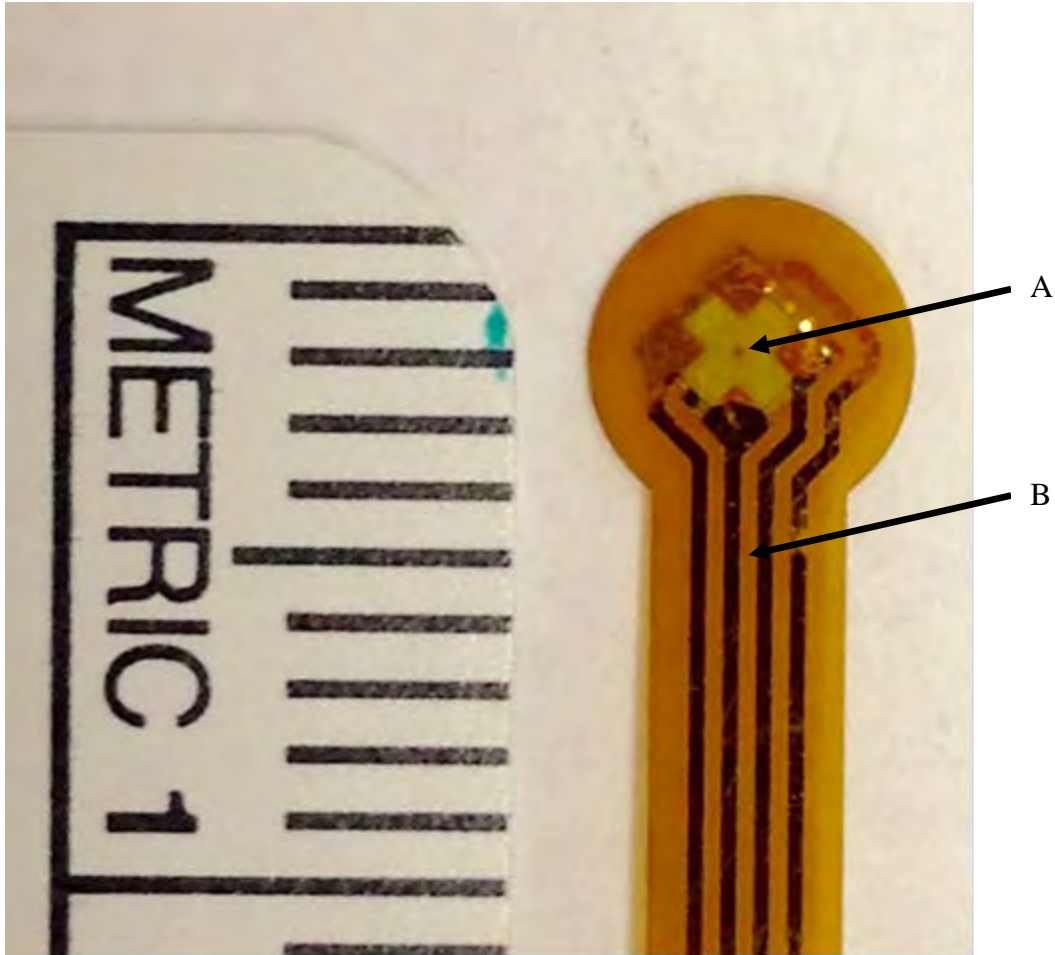


Figure2. Close-up photo of sensor showing diaphragm (A) and 4 connector contact strips (B).

Dr Kotovsky has machined a test chamber (Figure 3) that will provide a means of ex-vivo static and dynamic pressure testing. The chamber is a two part assembly with an aluminum base and clear Plexiglas top with a 2 mm^3 internal volume that simulates the volume of an adult rats brain. One inlet and one outlet port allow for filling with distilled water and efficient removal of air bubbles. The inlet port is a female Luer fitting that also allows for application of static pressure for calibration as well as connection to the fluid percussion device for dynamic testing. Initial static pressure calibration provided a linear response from 5 to 25 PSI (Figure 4). Further static calibrations will encompass a wider range of pressures and will be performed on the different diameter diaphragm units.

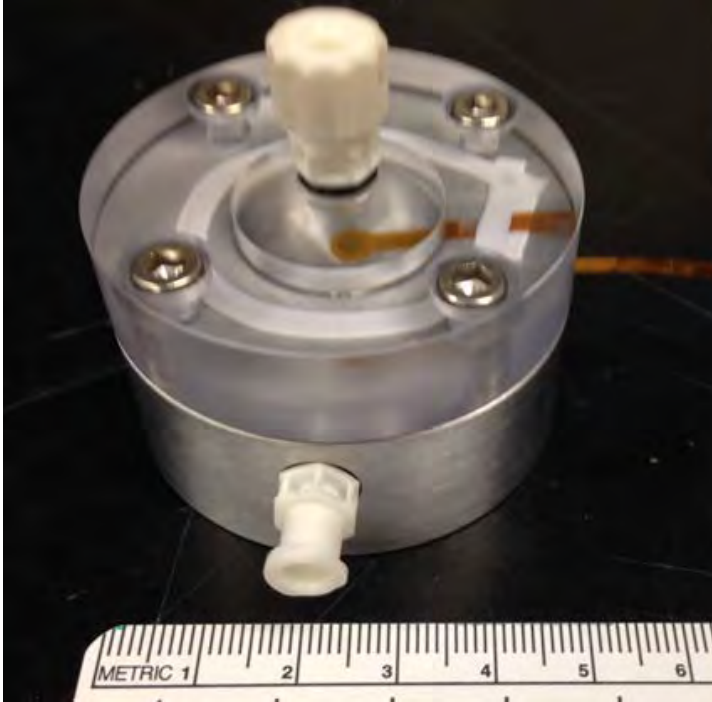


Figure 3. Test chamber for ex-vivo testing and calibration of sensors.

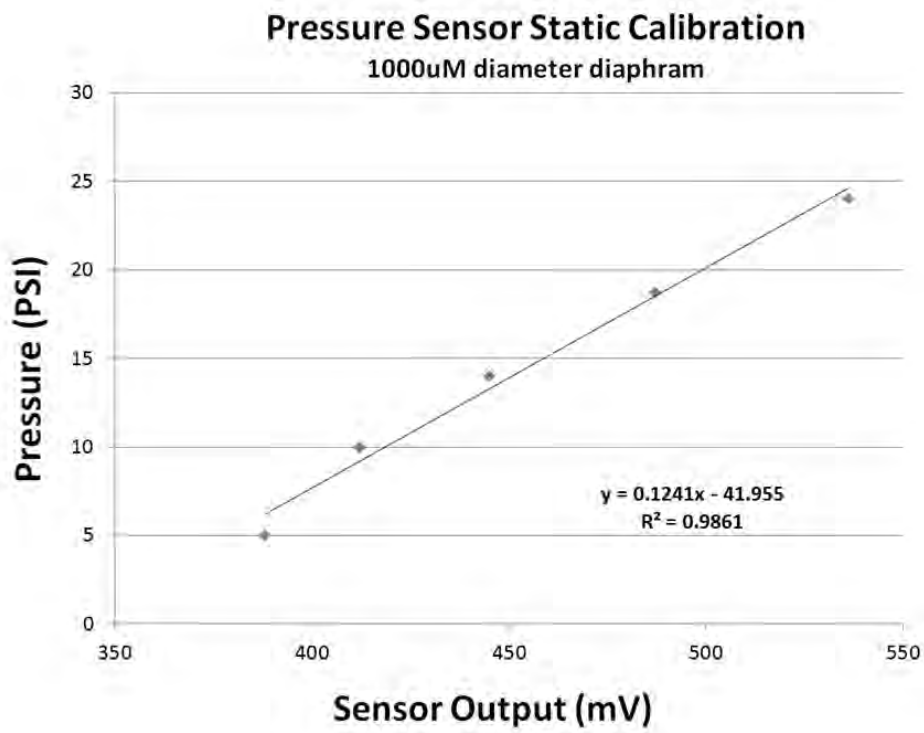


Figure 4. Static calibration of 1000 mm diameter diaphragm sensor.

We have performed an initial dynamic pressure comparison of the new 1000 μm sensor to the existing pressure transducer on the fluid percussion device (Figure 5) using the new test chamber connected to the fluid percussion device. The new sensor tracked changes in pressure over time that were in close agreement with the existing pressure transducer on the fluid percussion device. These results indicated that we need to provide shielding of the wires and connections to decrease electrical noise.

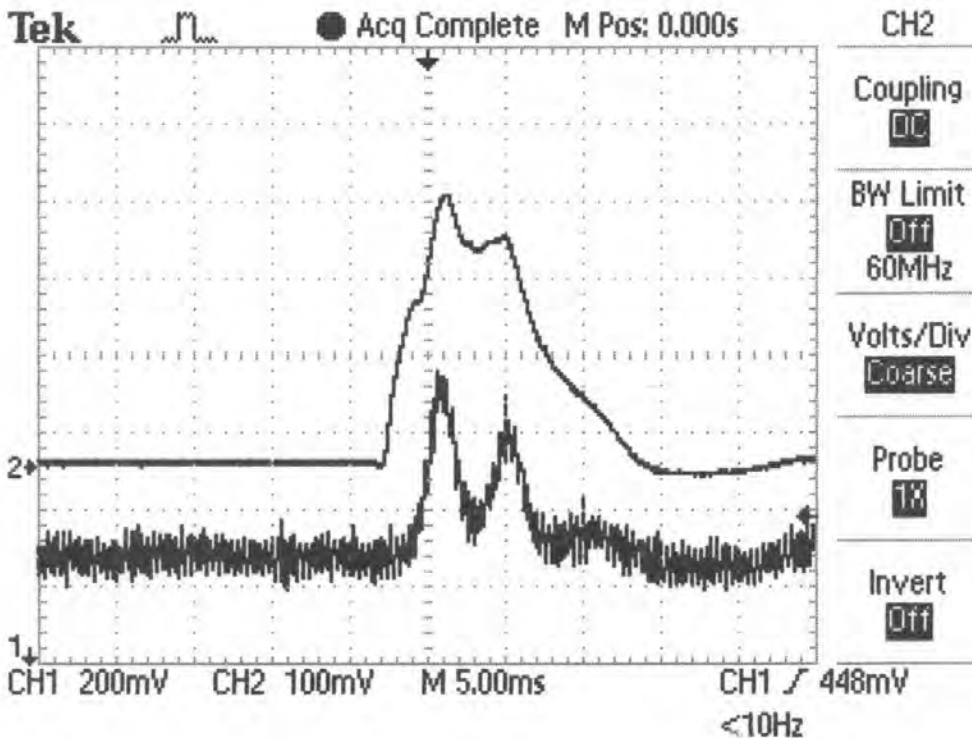


Figure 5. Dynamic comparison of fluid percussion pressure transducer (upper trace) and new 1000 μm diameter diaphragm sensor (lower trace)..

Key research accomplishments in the past year include:

- The first production of closed diaphragm wafer sensors were received from Lawrence Livermore National Laboratories and immediately tested.
- Static calibration produced a linear relationship between 5 and 25 PSI with an $R^2 = 0.986$
- The closed-diaphragm sensor is 90 microns thick and the final product with Kapton packaging is 130 microns thick
- Dynamic comparison of the new sensor with the existing fluid percussion pressure transducer provided close tracking of pressure events.
- Initial testing revealed the need for shielding of cables and power supply for subsequent applications.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?

In the remaining time of our current no-cost extension, we plan to perform thorough static pressure calibrations for each of the different diameter diaphragm sensors, followed by dynamic comparisons with the standard fluid percussion ex vivo pressure transducer. We will proceed with in situ animal testing with the sensor (e.g., 200 vs. 1000 μm diameter diaphragm) that produces the optimal sensitivity and range. We also plan to further refine the sensors into a smaller overall package and to design and implement a more user-friendly connection between the sensor and the recording instruments in order to make a smooth transition into making measurement in a blast TBI model later on in the project. We intend to continue working with a private company interested in the technology who may become a commercial outlet for general use of the sensors for TBI and potentially other studies. We look forward to bringing the sensor to commercialized success.

Reportable Outcomes:

- Static calibration of the new 1000 μm diaphragm sensors produced a linear relationship between 5 and 25 PSI with an $R^2 = 0.986$
- Dynamic comparison of the new sensor with the existing fluid percussion pressure transducer provided close tracking of pressure events

Impact:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

Changes/Problems

Nothing to Report

Products:

Nothing to Report

Participants & Other Collaborating Organizations:**What individuals have worked on the project?**

Name:	Bruce Lyeth, PhD
Project Role:	Principle Investigator
Researcher Identifier:	252972781 (UC Davis ID)
Nearest person month:	1
Contribution to the project:	Dr. Lyeth performed the calibrations of the new sensors
Funding Support:	No other source

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Lawrence Livermore National Laboratories
Livermore, CA
Partner makes the sensors

Special Reporting Requirements:**Collaborative Awards:**

Not applicable

Quad Chart:

Updated quad chart is attached.

Appendices:

None